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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/585,923	07/20/2006	Philippe Leissner	128639	1649

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EXAMINER	
PANDE, SUCHIRA	
ART UNIT	**PAPER NUMBER**
1637	

MAIL DATE	DELIVERY MODE
09/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/585,923	LEISSNER ET AL.	
	Examiner	Art Unit	
	SUCHIRA PANDE	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *1-5,10,11,13 and 14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-9,12 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/12/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group III invention (claims 6-9, 12 and 15) along with election of a pair of primers identified by SEQ ID NOs 1 and 2 in the reply filed on June 13, 2008 is acknowledged. The traversal is on the ground(s) that the office has failed to make a prima facie case that there is lack of unity of invention between claimed primer pairs. This is not found persuasive because claim 6 is drawn to *an amplification primer* not a primer pair. Prior art cited Kmiec et al. teaches a sequence that is 100% identical to the sequence of primer SEQ ID NO 1. Thus the product of claim 6 was taught to one of ordinary skill in the art at the time of the invention. Hence the product of group III invention, does not share same or corresponding special technical features of the methods of Group I and Group II inventions. Hence Unity of invention is lacking. In addition, each polynucleotide identified by different SEQ ID by definition represents a unique sequence with different characteristics and chemical properties associated with it conferred to it by that unique sequence, therefore each SEQ ID of the primer has to be searched individually. The invention requires use of a primer pair, therefore the elected pair of primers identified by their SEQ IDs properly constitute a restriction subgroup. The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-5, 10-11, 13-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable

generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on June 13, 2008.

Claim Status

3. Consistent with above elections claims 6-9, 12 and 15 will be examined to the extent they read upon the elected primer pair SEQ ID NOs 1 and 2 in this action.

Priority

4. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified English translation of PCT/FR0450257 with priority date of 2/12/2004 has not been received. Accordingly for prior art purposes the priority of the instant application is the filing date of the PCT/FR2005/050083 which is 2/10/2005.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on 9/12/06 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 6, 7 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Bertina et al. WO 95/21938 published on 18 August 1995.

Regarding claim 6, Bertina et al. teach an amplification primer comprising at least 15 nucleotide units of a nucleotide sequence chosen from SEQ ID NOs: 1, 2 (see page 46 Table 5 where Primer P2 is taught. Primer P2 is 100% identical to SEQ ID NO 2 of instant application). The alignment is provided below.

```
RESULT 1
AAT03933
ID   AAT03933 standard; DNA; 22 BP.
XX
AC   AAT03933;
XX
DT   20-DEC-1995  (first entry)
XX
DE   Factor-V NASBA primer P2.
XX
KW   Factor-V; thrombosis; thrombophilia; diagnosis; anticoagulant;
KW   activated protein-C; APC; homozygosity; heterozygosity; primer;
KW   nucleic acid sequence based amplification; NASBA; ss.
XX
OS   Synthetic.
XX
PN   WO9521938-A1.
XX
PD   17-AUG-1995.
XX
PF   14-FEB-1995;   95WO-EP000553.
XX
PR   14-FEB-1994;   94EP-00200377.
XX
PA   (UYLE-) RIJKSUNIV LEIDEN.
XX
PI   Bertina RM,  Reitsma PH;
XX
DR   WPI; 1995-293134/38.
XX
PT   Screening for genetic defect associated with thrombosis and/or poor
PT   anticoagulant response to activated protein C - useful to determine
PT   homozygosity or heterozygosity for a mutation in Factor V, Va, VIII or
PT   VIIIa.
XX
PS   Example 3; Page 46; 98pp; English.
XX
CC   The amplification primers and detection probes given in AAT03932-38 are
CC   used for NASBA of human Factor-V DNA in order to detect a mutation at
CC   codon 506 associated with an increased risk of thrombotic events. Primer
CC   P2 is located in exon 11 of the Factor V coding sequence
XX
SQ   Sequence 22 BP; 9 A; 5 C; 3 G; 5 T; 0 U; 0 Other;
```

```
  Query Match             100.0%;  Score 22;  DB 2;  Length 22;
  Best Local Similarity   100.0%;  Pred. No. 0.35;
  Matches   22;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps
0;

Qy          1 AGTGCTTAACAAGACCATACTA 22 SEQ ID NO 2
              ||||||||||||||||||||||
Db          1 AGTGCTTAACAAGACCATACTA 22 Primer P2 of Bertina et al.
```

Regarding claim 7, Bertina et al. teach a promoter allowing the initiation of transcription by a T7 bacteriophage polymerase (see page 45 Example 3 where transcription by a T7 bacteriophage polymerase is taught. Thus the construct inherently contains a promoter allowing the initiation of transcription by a T7 bacteriophage polymerase. Thus Bertina et al. teach a promoter allowing the initiation of transcription by a T7 bacteriophage polymerase).

Regarding claim 12, Bertina et al. teach a kit (see claim 39 where kit is taught) Thus all the elements of claims 6, 7 and 12 are anticipated by Bertina et al.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 8, 9 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bertina et al. WO 95/21938 published on 18 August 1995 in view of Kmiec et al. (US pat. 6, 936, 467 B2 filed on March 27, 2001)

Regarding claim 8, Bertina et al. teach a pair of amplification primers (see page 46 table 5 where primer pair P1 and P2 are taught) chosen from the following pairs of primers:

a second amplification primer comprising at least 15 nucleotide units of the nucleotide sequence SEQ ID NO: 2 (see page 46 Table 5 where Primer P2 is taught. Primer P2 is 100% identical to SEQ ID NO 2 of instant application). The alignment is provided above for claim 6.

Regarding claim 8, Bertina et al. teach a first amplification primer (see Primer P1 in Table 5). Regarding claim 8, Bertina et al. teach do not teach a first amplification primer comprising at least 15 nucleotide units of the nucleotide sequence SEQ ID NO: 1.

Regarding claim 8, Kmiec et al. teach a first amplification primer comprising at least 15 nucleotide units of the nucleotide sequence SEQ ID NO: 1. See alignment shown below where Kmiec et al. teaches a product namely a sequence that is 121 nucleotides long and comprises an oligonucleotide that is 100% identical to the oligonucleotide claimed as SEQ ID no 1 in the instant application.

```
AR711557
LOCUS       AR711557                121 bp    DNA     linear   PAT 21-SEP-
2005
DEFINITION  Sequence 1789 from patent US 6936467.
ACCESSION   AR711557
REFERENCE   1  (bases 1 to 121)
  AUTHORS   Kmiec,E.B., Gamper,H.B. and Rice,M.C.
  TITLE     Targeted chromosomal genomic alterations with modified single
            stranded oligonucleotides
  JOURNAL   Patent: US 6936467-A 1789 30-AUG-2005;
            University of Delaware; Newark, DE

  Query Match             100.0%;  Score 23;  DB 2;  Length 121;
  Best Local Similarity   100.0%;  Pred. No. 0.79;
  Matches   23;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps
0;

Qy          1 AAATTCTCAGAATTTCTGAAAGG 23 SEQ ID no 1 claimed
              |||||||||||||||||||||||
Db          7 AAATTCTCAGAATTTCTGAAAGG 29 SEQ ID 1789 of Prior art


Factor V mutation correcting oligonucleotide SEQ ID NO: 1789.
```

Thus Kmiec et al. teaches a first amplification primer comprising at least 15 nucleotide units of the nucleotide sequence SEQ ID NO: 1.

Regarding claim 9, Bertina et al. teach a promoter allowing the initiation of transcription by a T7 bacteriophage polymerase (see page 45 Example 3 where transcription by a T7 bacteriophage polymerase is taught. Thus the construct contains a promoter allowing the initiation of transcription by a T7 bacteriophage polymerase. Thus Bertina et al. teach a promoter allowing the initiation of transcription by a T7 bacteriophage polymerase).

Regarding claim 15, Bertina et al. teach a kit (see claim 39 where kit is taught).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the primer of SEQ ID NO 1 taught by Kmiec et al. with the primer of SEQ ID NO: 2 taught by Bertina et al.

The motivation to do so is provided to one of ordinary skill by teachings of both Kmiec et al. and Bertina et al.

Bertina et al. teach use of NASBA an amplification method that utilizes transcription of RNA by using T7 RNA polymerase (see Example 3 pages 45-46) for amplification of factor V gene. The primers P1 and P2 taught by Bertina et al. are used as amplification primers used for NASBA of human Factor-V DNA in order to detect a mutation at codon 506 associated with an increased risk of thrombotic events. Primer P2 is located in exon 11 of the Factor V coding sequence (see the information provided above for claim 6 with the sequence alignment).

Kmiec et al. teaches an oligonucleotide no 1789 that is used to correct for a mutation in Factor V gene. The deficiency of factor V is caused by stop codons TGA in the genomic DNA. The oligo used to correct the deficiency changes TGA to CGA thus changing the stop codon to an Arginine (see col. 135 and 136 SEQ ID no 1789). The oligo of Primer identified by SEQ ID NO 1 in the instant application is sequence upstream of this critical position at amino acid 506. If it is a stop codon TGA then subject will be deficient in factor V. If the codon at that position is CGA then subject will have no factor V deficiency).

Given this knowledge one of ordinary skill in the art is capable of designing primers from upstream region of the 506 amino acid position that will have the T7 promoter sequence to used as first primer and use the primer of SEQ ID NO 2 taught by Bertina et al. as downstream primer for use in NASBA amplification. By doing so one of ordinary skill in the art has a pair of primers in hand that can be used in NASBA

amplification and can help determine if the patient carries a normal or mutant allele at position 506 of factor V. It is apparent to one of ordinary skill in the art that if these primer pairs are packaged in a kit then the medical technician is less likely to make an error while setting up the amplification reactions. To screen for presence of normal or mutant allele of factor V gene in the patient sample the technician needs to use the primer pairs identified by SEQ ID NO 1 and 2 so as to amplify the region of factor V gene that is involved in Factor V deficiency.

Conclusion

11. All claims under consideration 6-9, 12 and 15 are rejected over prior art.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUCHIRA PANDE whose telephone number is (571)272-9052. The examiner can normally be reached on 8:30 am -5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Suchira Pande
Examiner
Art Unit 1637

/Teresa E Strzelecka/

Primary Examiner, Art Unit 1637

September 9, 2008